



48,XXYY syndrome

48,XXYY syndrome is a chromosomal condition that causes medical and behavioral problems in males.

48,XXYY disrupts male sexual development. Adolescent and adult males with this condition typically have small testes that do not produce enough testosterone, which is the hormone that directs male sexual development. A shortage of testosterone during puberty can lead to reduced facial and body hair, poor muscle development, low energy levels, and an increased risk for breast enlargement (gynecomastia). Because their testes do not function normally, males with 48, XXYY syndrome have an inability to father children (infertility).

48,XXYY syndrome can affect other parts of the body as well. Males with 48,XXYY syndrome are often taller than other males their age. They tend to develop a tremor that typically starts in adolescence and worsens with age. Dental problems are frequently seen with this condition; they include delayed appearance of the primary (baby) or secondary (adult) teeth, thin tooth enamel, crowded and/or misaligned teeth, and multiple cavities. As affected males get older, they may develop a narrowing of the blood vessels in the legs, called peripheral vascular disease. Peripheral vascular disease can cause skin ulcers to form. Affected males are also at risk for developing a type of clot called a deep vein thrombosis (DVT) that occurs in the deep veins of the legs. Additionally, males with 48,XXYY syndrome may have flat feet (pes planus), elbow abnormalities, allergies, asthma, type 2 diabetes, seizures, and congenital heart defects.

Most males with 48,XXYY syndrome have some degree of difficulty with speech and language development. Learning disabilities, especially reading problems, are very common in males with this disorder. Affected males seem to perform better at tasks focused on math, visual-spatial skills such as puzzles, and memorization of locations or directions. Some boys with 48,XXYY syndrome have delayed development of motor skills such as sitting, standing, and walking that can lead to poor coordination. Affected males have higher than average rates of behavioral disorders, such as attention deficit hyperactivity disorder (ADHD); mood disorders, including anxiety and bipolar disorder; and/or autism spectrum disorders, which affect communication and social interaction.

Frequency

48,XXYY syndrome is estimated to affect 1 in 18,000 to 50,000 males.

Genetic Changes

48,XXYY syndrome is a condition related to the X and Y chromosomes (the sex chromosomes). People normally have 46 chromosomes in each cell. Two of the 46 chromosomes, known as X and Y, are called sex chromosomes because they help determine whether a person will develop male or female sex characteristics. Females typically have two X chromosomes (46,XX), and males have one X chromosome and one Y chromosome (46,XY). 48,XXYY syndrome results from the presence of an extra copy of both sex chromosomes in each of a male's cells (48,XXYY). Extra copies of genes on the X chromosome interfere with male sexual development, preventing the testes from functioning normally and reducing the levels of testosterone. Many genes are found only on the X or Y chromosome, but genes in areas known as the pseudoautosomal regions are present on both sex chromosomes. Extra copies of genes from the pseudoautosomal regions of the extra X and Y chromosome contribute to the signs and symptoms of 48,XXYY syndrome; however, the specific genes have not been identified.

Inheritance Pattern

This condition is not inherited; it usually occurs as a random event during the formation of reproductive cells (eggs and sperm). An error in cell division called nondisjunction results in a reproductive cell with an abnormal number of chromosomes. In 48,XXYY syndrome, the extra sex chromosomes almost always come from a sperm cell. Nondisjunction may cause a sperm cell to gain two extra sex chromosomes, resulting in a sperm cell with three sex chromosomes (one X and two Y chromosomes). If that sperm cell fertilizes a normal egg cell with one X chromosome, the resulting child will have two X chromosomes and two Y chromosomes in each of the body's cells.

In a small percentage of cases, 48,XXYY syndrome results from nondisjunction of the sex chromosomes in a 46,XY embryo very soon after fertilization has occurred. This means that an normal sperm cell with one Y chromosome fertilized a normal egg cell with one X chromosome, but right after fertilization nondisjunction of the sex chromosomes caused the embryo to gain two extra sex chromosomes, resulting in a 48,XXYY embryo.

Other Names for This Condition

- XXYY syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: XXYY syndrome
<https://www.ncbi.nlm.nih.gov/gtr/conditions/C2936741/>

General Information from MedlinePlus

- Diagnostic Tests
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation
<https://medlineplus.gov/surgeryandrehabilitation.html>

Additional Information & Resources

MedlinePlus

- Health Topic: Attention Deficit Hyperactivity Disorder
<https://medlineplus.gov/attentiondeficithyperactivitydisorder.html>
- Health Topic: Male Infertility
<https://medlineplus.gov/maleinfertility.html>
- Health Topic: Tooth Disorders
<https://medlineplus.gov/toothdisorders.html>
- Health Topic: Tremor
<https://medlineplus.gov/tremor.html>

Genetic and Rare Diseases Information Center

- 48,XXYY syndrome
<https://rarediseases.info.nih.gov/diseases/5677/48xyy-syndrome>

Additional NIH Resources

- National Institute of Diabetes and Digestive and Kidney Diseases: Diabetes
<https://www.niddk.nih.gov/about-niddk/research-areas/diabetes/Pages/diabetes.aspx>

Educational Resources

- American Heart Association: What Is Peripheral Vascular Disease?
http://www.heart.org/idc/groups/heart-public/@wcm/@hcm/documents/downloadable/ucm_300323.pdf
- Boston Children's Hospital: Autism Spectrum Disorders
<http://www.childrenshospital.org/conditions-and-treatments/conditions/autism-spectrum-disorders>
- Boston Children's Hospital: Congenital Heart Defects
<http://www.childrenshospital.org/conditions-and-treatments/conditions/congenital-heart-defects>
- Boston Children's Hospital: Learning Disorders and Disabilities
<http://www.childrenshospital.org/conditions-and-treatments/conditions/learning-disorders-and-disabilities>
- MalaCards: 48,xxyy syndrome
http://www.malacards.org/card/48xxyy_syndrome
- March of Dimes: Chromosomal Conditions
<http://www.marchofdimes.org/baby/chromosomal-conditions.aspx>
- Orphanet: 48,XXYY syndrome
http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=10
- TeensHealth: Delayed Puberty
<http://kidshealth.org/en/teens/delayed-puberty.html>

Patient Support and Advocacy Resources

- Association for X and Y Chromosome Variations
<https://genetic.org/>
- RESOLVE: The National Infertility Association
<http://www.resolve.org/>
- The XXYY Project
<http://xyysyndrome.org/main/>
- University of Kansas Medical Center Resource List: Infertility
<http://www.kumc.edu/gec/support/inferti.html>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%2848,+XXYY%5BTIAB%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

Sources for This Summary

- Tartaglia N, Borodyanskaya M, Hall DA. Tremor in 48,XXYY syndrome. *Mov Disord*. 2009 Oct 15;24(13):2001-7. doi: 10.1002/mds.22700. Erratum in: *Mov Disord*. 2010 Aug 15;25(11):1764. Borodyanskaya, Mariya [corrected to Borodyanskaya, Mariya].
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19705466>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3056502/>
 - Tartaglia N, Davis S, Hench A, Nimishakavi S, Beauregard R, Reynolds A, Fenton L, Albrecht L, Ross J, Visootsak J, Hansen R, Hagerman R. A new look at XXYY syndrome: medical and psychological features. *Am J Med Genet A*. 2008 Jun 15;146A(12):1509-22. doi: 10.1002/ajmg.a.32366.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/18481271>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3056496/>
 - Visootsak J, Graham JM Jr. Klinefelter syndrome and other sex chromosomal aneuploidies. *Orphanet J Rare Dis*. 2006 Oct 24;1:42. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17062147>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1634840/>
 - Visootsak J, Rosner B, Dykens E, Tartaglia N, Graham JM Jr. Behavioral phenotype of sex chromosome aneuploidies: 48,XXYY, 48,XXXY, and 49,XXXXY. *Am J Med Genet A*. 2007 Jun 1; 143A(11):1198-203.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17497714>
 - Zelante L, Piemontese MR, Francioli G, Calvano S. Two 48,XXYY patients: clinical, cytogenetic and molecular aspects. *Ann Genet*. 2003 Oct-Dec;46(4):479-81.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/14659786>
-

Reprinted from Genetics Home Reference:

<https://ghr.nlm.nih.gov/condition/48xxyy-syndrome>

Reviewed: January 2010

Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services